agus. The exact prevalence is not known, but Barrett's esophagus is found in about 10% of patients undergoing esophagoscopy for symptoms of reflux.

On histologic examination, Barrett's esophagus has a heterogeneous appearance and comprises a variety of cell types similar to gastric and intestinal epithelial cells. A distinctive histologic pattern of goblet cells interspersed among columnar mucous cells is common and virtually diagnostic of Barrett's esophagus. Other patterns resemble gastric fundic or cardiac mucosa and can thus be interpreted as Barrett's esophagus only when the site of biopsy is definitely the esophagus and not a hiatus hernia.

This condition is clinically important because of its association with esophageal adenocarcinoma. In recent studies, a 30 to 40 times increased risk was estimated when Barrett's esophagus is present. Because these figures are based on a relatively short follow-up period, the actual risk may be even higher. Such considerations have led to the suggestion that biopsies be done regularly on patients with Barrett's esophagus to look for epithelial dysplasia, which, as a putative precursor of adenocarcinoma, would serve to identify those patients at highest risk for malignancy. Problems with this suggestion include the lack of well-defined histologic criteria for recognizing dysplasia and distinguishing it from reactive or regenerative changes. Nevertheless, high-grade dysplasia has recently been shown to represent a morphologic marker of risk for esophageal adenocarcinoma.

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The Carcinoma-Carcinoid Spectrum

IN THE PAST DECADE we physicians have become aware that carcinoid tumors show a much wider clinicopathologic spectrum than previously thought. This has given rise to a plethora of new terms, some of which, such as apudoma, neurochristoma and neuroendocrinoma, are based on their postulated neuroectodermal derivation; others, such as neuroendocrine carcinoma, on their clinical behavior, and a group, such as gastrinoma, on their secretion products. Because these tumors are morphologically distinctive, I see no point in changing Obendorfer's original terminology, and thus I designate these lesions as carcinoids and specify their differentiation and secretion products (Table 1).

On histologic examination, some tumors may show atypical features such as glandular profiles, a spindle cell pattern, squamous or osteoid metaplasia or pleomorphism with frequent mitoses and necrosis. In rare cases they may be poorly differentiated and resemble undifferentiated large-cell or small-cell carcinoma (oat cell carcinoma) and lymphoma. As is well known, some carcinoids are associated with well-defined syndromes, such as the carcinoid or the Zollinger-Ellison syndromes, due to the secretion of amines or peptides. Immunohistochemical analysis of these tumors has shown that, whereas one amine or peptide may predominate, such as serotonin or gastrin, most are multihormonal. These findings

TABLE 1.—*Nomenclature and Classification of Pure and Mixed Endocrine Cell Tumors*

Carcinoid tumors
Well differentiated
Moderately differentiated
Poorly differentiated
Small cell (oat cell)
Large cell
Mixed (composite) glandular-endocrine cell carcinoma
Microglandular-goblet cell carcinoma
Scirrhous-argyrophil cell carcinoma
Adenoendocrine cell carcinoma
Amphicrine cell carcinoma

are also seen with the clinically silent carcinoids such as the foregut and hindgut tumors. Furthermore, the immunohistochemically shown amines and peptides in the primary tumor do not necessarily correspond to those found in the overlying endocrine cells or in metastatic lesions.

Although the presence of scattered endocrine cells within adenomas and carcinomas of the gastrointestinal tract has been known for some time (in as many as 20% of all colonic carcinomas), there are a number of tumors in which there is a large admixture of endocrine and epithelial cells. Thus, the strict separation of gut mucosal tumors into carcinoma and endocrine tumors has had to be modified to include those tumors with admixtures of varying proportions of endocrine and epithelial cells. These tumors have been designated as mixed or composite tumors and have been further subdivided into several distinctive histologic types (see Table 1). Some of these tumors, such as the microglandular-goblet cell carcinoma, have a distinctive clinical behavior, whereas others, such as the scirrhous-argyrophil and adenoendocrine cell carcinoma, appear to behave in a manner similar to the corresponding carcinoma. Finally, there is a further distinctive tumor type, namely the amphicrine tumors. These differ from the mixed tumors in that endocrine and epithelial cell constituents are present within the same cell. These findings support the hypothesis that epithelial and endocrine cells of the gut share a common cell of origin.

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Lymphocyte Gene Rearrangements—A New Technique in the Diagnosis of Lymphoma

THE HISTOPATHOLOGIC DIAGNOSIS of lymphoma can be difficult, particularly when the disease presents at extranodal sites. Conventional microscopic or immunohistochemical studies often prove inadequate for the evaluation of T-cell infiltrates, of neoplasms lacking appreciable atypia or where a superimposed inflammatory process obscures the underlying malignant process.

Recent insights into the molecular biology of lymphocytes have led to the development of a technique that provides an objective estimate of the clonal composition of lymphoid in-